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PHYSIOLOGY OF WATER AND SODIUM CHLORIDE **/62

O.Cohnheim, G.Kreglinger, L.Tobler, and O.H.Weber*

Results of experiments on sodium chloride excretion of the human organism at high altitudes, at physical exertion and at rest, with low- and high-salt diets, are discussed. Sodium chloride depletion and concomitant permanent weight loss was observed only at profuse perspiration. Excessive chlorine loss led to reduction of gastric HCl secretion with resultant muscular fatiguability due to impaired deacidification of the tissues.

In the physiological and medical literature, treating the influence of altitude climate on human and animal organisms, considerable differences exist on the problem whether and in how far the number of red blood corpuscles and the amount of hemoglobin, per unit volume of the circulating blood, show an increase. In small animals such as rabbits, rats, and guinea pigs, a considerable increase in blood corpuscles has been observed already at elevations below 2000 m, by Miescher (Bibl.1 - 7) and his coworkers; all later researchers, among whom we merely mention Abderhalden, Foà, and Giacosa (Bibl.8 - 10), confirmed these findings. Abderhalden, in this type of animal, observed complete parallelism between the number of blood corpuscles and the hemoglobin content and found no difference between peripheral blood or blood taken from the large vessels. The

* From the Monte-Rosa Laboratories, Institute Mosso, Colle d'Olen, and Margherita Hut.

** Numbers in the margin indicate pagination in the original foreign text.

situation is entirely different in human subjects. Already the very first /63 investigators, belonging to Miescher's school, noted that there was by no means the same accurate regularity as that observed in rabbits. The increase in blood corpuscles seemed to be a fact, but no hemoglobin increase could be detected; this makes it rather difficult to understand that, for many years, erythrocytosis in human subjects had been considered an established fact and was used as the very basis of the physiological and even of the therapeutic altitude effect. The reliance on the blood counts was so great that special theories were invented to explain why the hemoglobin did not increase at the same rate as the erythrocytes. These theories were maintained even in the face of long-time strenuous refutations of the existence of erythrocytosis in the human organism at high altitudes. Pertinent investigations in this direction included those by Zuntz and his followers, according to whom the blood count in the peripheral blood was unreliable and who never were able to detect a definite increase (Bibl.11; with extensive literature references).

The contradictions with respect to the problem of erythrocytosis apparently were more or less reconciled in recent investigations by Bürker. This author (Bibl.12 - 15) demonstrated that the Thoma-Zeiss counter, used until then, produced excessive values at high elevations above sea level. This was obviously due to the fact that the evaporation is increased and the blood is concentrated during the necessarily slow work with the old-type counting chamber. For this reason, Bürker designed a new type of counter, with which he made detailed investigations and found that, at an elevation of 1800 m, a minor increase in /64 blood corpuscles in the human organism took place. In four experimental subjects, he first found a slight increase, followed by a decrease, and then again by a slow increase which reached a maximum within 3 - 4 weeks. The absolute increase was only 4 - 5%, which does exceed (but only slightly) the experimental error which, according to Bürker, is not more than 2.5%. It is quite obvious that an increase of this type would not be specifically regarded had it not been for the fact that, with the inadequate earlier methods, a greater increase had been recorded.

In earlier times, much greater increases had been observed at higher altitudes (Bibl.16; a further compilation of literature data for the Results of Physiology, 1912, by Cohnheim is in printing). However, these observations were not confirmed later; for example, certain data on a rapid increase in blood corpuscles during balloon ascents had to be corrected later (Bibl.17). Cohnheim and Kreglinger (Bibl.18) determined the hemoglobin content in human blood with the Haldane apparatus and found no increase at elevations of 2900 and 4500 m, within 12 days. The same instrument was used by Masing and Morawitz (Bibl.19) on the Colle d'Olen, by Douglas (Bibl.20) in Teneriffa, and by Ward (Bibl.21) on the Monte Rosa. Masing and Morawitz detected an increase of about 5%, while Douglas found that the oxygen combination increased from 18 to 20% for one of the observers and much less distinctly for the other. Ward reported that the hemoglobin content, which was on the average 101 in London, increased to 98 - 106 in Zermatt, and to 107 - 115 on the Margherita Hut. This means that slight increases are recorded even with these determination methods, although there are always intermediate values that show no increase whatsoever. However, since other authors [for example, Fuchs (Bibl.22)] reported a hemoglobin rise /65 in human subjects in high mountains, we believed it advisable to make simultaneous determinations of erythrocyte number and hemoglobin amount at high altitudes, using different methods, so as to eliminate or explain the discrepancies.

From July 31 to August 13, 1911, we stayed at the Colle d'Olen Laboratory and, a part of this time (Aug.3 - 6), at the Margherita Hut. We wish to express our appreciation at this point to the director of the Institute Mosso, Dr.Aggazzotti, for his accommodating and willing cooperation. We also are grateful to the German and Austrian Alpine Club for a financial contribution. This enabled us to simultaneously use and compare the more important apparatus for determining the blood concentration.

For future visitors to the Institute Mosso it might be of interest that we donated all apparatus to the director of the Institute and that the Laboratory now possesses, in addition to the old-type Thoma-Zeiss counter, the recent modification by Bürker as well as the Sahli, Haldane, Autenrieth, Königsberger, and Grützner apparatus.

The participants in the experiments were:

O.Cohnheim, age 38, height 171 cm, weight 84 kg;

G.Kreglinger, age 59, height 186 cm, weight 78 kg;

L.Tobler, age 34, height 175 cm, weight 65 kg;

O.Weber, age 35, height 166 cm, weight 64 kg.

All of us were used to the mountains, but were entirely untrained at the beginning of the experiments.

The blood tests were first made on ourselves. We usually took the blood from the fingertip. The cut, with the scarifier, was made sufficiently large to obtain an amount of blood sufficient for 4 or 5 simultaneous determinations. /166 The first drop of blood was discarded. We are convinced that this was the best manner for determining the true hemoglobin content of the circulating blood, but refer here also to the determinations by Cohnheim and Kreglinger according to whom either maximum or minimum blood circulation in the skin (effect of heat or cold) has no influence on the hemoglobin value of the sampled blood. We would like to mention specifically that this accuracy probably is true only for the fingertip which contains many more blood vessels than most other parts of the skin. The fingertip has such a dense capillary network that it is immaterial if actually a few vasa serosa were interspersed here; incidentally, such vasa were never reliably observed in human subjects. It is known that the fingertips also contain arteriovenous anastomoses, which could be pierced accidentally.

The blood count (Tobler) was made with the Bürker counter, always counting 100 squares. Of the hemoglobin determination methods used by us, we believe that the most reliable values are obtained with the Haldane apparatus in which case, however, it must be taken into consideration that one of us who made these determinations (Cohnheim) was especially familiar with the apparatus. The recent objection against the reliability of the Haldane method, raised by Barcroft (Bibl.23 - 25) in his newest findings, is not valid since the maximum saturation of hemoglobin with carbon monoxide is not influenced by the variations in the dissociation curve described by Barcroft. Naturally, no manufactured gas was available at the Colle d'Olen; we prepared carbon monoxide by heating oxalic acid with sulfuric acid and absorbing the carbon dioxide in caustic soda solution; the gas was stored in a flask from which we removed it by means of a pipette. This permitted determinations also outside of the Laboratory. The readings are direct values and, as is generally known, refer to a normal content of the blood of 100. We had two test tubes and two control tubes available, which all gave the same values. /67

For the determinations with Sahli's apparatus (Kreglinger, Tobler), we had two units available. It is known that Sahli's apparatus is so calibrated that the number 80 refers to normal hemoglobin content. We have given the actual readings but also converted them at a ratio of 80:100, to permit a convenient comparison with the Haldane figures. It was found that the agreement was excellent in the majority of cases. Bürker (Bibl.26), calibrated the Sahli apparatus to absolute hemoglobin content and reported that the absolute hemoglobin content is obtained on multiplying the reading by 0.173. For a value of 80, this gives a hemoglobin content of 13.8%. The Haldane apparatus is so calibrated that its value of 100 corresponds to an oxygen combining power of 18.5%. It is known that 1 gm hemoglobin combines 1.34 cc oxygen, so that a hemoglobin content of 13.8% will be obtained for the value of 100 in the Haldane apparatus. The agreement with Bürker's calibration is excellent.

In Sahli's apparatus, the hemoglobin is converted by hydrochloric acid into hematin, which is then compared with a standard solution. The same principle is used for a newly developed apparatus by Autenrieth and Königsberger (Bibl.27, 28). In this method, 20 cc blood are mixed with hydrochloric acid. The liquid is then poured into a small vessel with straight walls which is always filled to a certain mark; the measurement proceeds as in the Grützner apparatus, by moving a standard wedge back and forth until both the wedge and the vessel with the hematin show the same light color. The displacement of the wedge is read off from a scale, and the corresponding hemoglobin value is taken from a chart furnished with the apparatus. It is also possible to calibrate the apparatus by /68
other methods. The graph, accompanying the apparatus, is normed to the Sahli apparatus so that the hemoglobin standard is 80. We preferred to give the values for the standard of 100. As in all colorimetric determinations, one must be familiar with the type of apparatus used. After some training, we obtained highly accurate readings. Since a gradual addition of liquid to the blood solution is unnecessary here, the apparatus is much more convenient and presents fewer error sources than the other instruments. The only drawback might be the

considerable width of the reservoir, since special care must be taken to have this reservoir standing level when filling it. Another, more important, objection is that raised by Stäubli (Bibl.29). He found that, because of the considerable excess of hydrochloric acid, a darkening of the solution takes place so that the values will differ, depending on whether the reading was taken immediately after sampling or sometime later. Whether a reduction in the amount of hydrochloric acid might eliminate this difficulty cannot be decided at present. By chance, our own experiments were always so arranged that we took the last readings on the Autenrieth and Königsberger apparatus, which meant that the risk of darkening of the solution was not excessive. Individual values that differed completely from the others could possibly be explained in this manner; however, otherwise the agreement was satisfactory.

The results of the blood tests are compiled in Table I. The determinations in Lausanne were made in the early morning on arising. We arrived by train in Varallo on the afternoon of July 30, and the first determinations were made immediately thereafter, several hours after the last meal. The ascent from Alagna to the Colle d'Olen took place on the afternoon and evening of July 31, and the first determination atop the mountain was made in the forenoon of the next day. This took place 4 hrs after breakfast, following some laboratory work. All /69
later determinations on the Colle d'Olen and at the Margherita Hut were made under the same conditions, with the exception of a few determinations at the Hut which were made immediately after a strenuous climb.

These blood tests showed no noticeable increase in hemoglobin and erythrocytes at high elevations. Within a period of 12 days, the increase was so negligible that it did not exceed the error limits. We also made a blood test on Dr.Aggazzotti who, at that time, had been staying at the Colle d'Olen for about three weeks. This test showed the following result·

Haldane	105
Sahli	84:105
	84:105
Autenrieth and Königsberger	26:102
Erythrocytes	5,432,000.

No results of blood tests in the lowland were available for Dr.Aggazzotti, but the data were the same as those obtained on ourselves and the same as expected of a healthy, fairly young male at sea level.

In addition, we took blood tests of two dogs. Cohnheim and Kreglinger postulated the hypothesis that the considerable discrepancy with respect to rise in hemoglobin, existing between rabbits and human subjects, must be due to the differing evolution of the water metabolism. Because of the increased evaporation at higher altitudes, a greater physical water loss must occur in all animals that breathe through the lungs. In the human organism which, because of the perspiration, is adjusted to water losses, this loss is immediately compensated. In rabbits, however, which have no water dissipation for purposes of heat removal, such a regulatory mechanism is absent or so poorly developed that any water loss will lead to hemoconcentration. This assumption would satisfactorily explain all observed facts. For a further check, it seemed desirable to make experiments on dogs, an animal that is able to increase its water dissipation /70 for purposes of heat removal by accelerated panting. In the dog, the water dissipation takes place as promptly as in man, but in a different manner. In other animals, such as in hogs and cattle, Abderhalden detected a concentration of the blood at higher altitudes, but to a much lesser extent than in rabbits and rats. These animals are so large that they, no doubt, have a physical heat regulation;

TABLE I

	Kreglinger				Cohnheim				Tobler				Weber			
	Hal-dane	Sahli	A. and K.	Erythro-cytes	Hal-dane	Sahli	A. and K.	Erythro-cytes	Hal-dane	Sahli	A. and K.	Erythro-cytes	Hal-dane	Sahli	A. and K.	Erythro-cytes
Heidelberg, 100 m, July 26	—	—	—	—	102	80 = 100	29 = 89	4,832,000	—	—	29 = 99	4,504,000	—	—	—	—
Heidelberg, 100 m, July 27	—	—	—	—	—	—	—	4,496,000	—	85 = 106	26 = 103	4,608,000	—	—	—	—
Lausanne, 483 m, July 30	106	81 = 101	32 = 97	—	106	86 = 107	—	—	—	—	—	—	—	—	—	—
Varallo, 451 m, July 30	86	83 = 104 80 = 100	32 = 97	—	106	86 = 107	—	—	—	—	80 = 100	—	100	—	24 = 105	—
Colle d'Olen, 2900 m, Aug. 1	95	70 = 88	31 = 97	5,040,000	98	78 = 98	—	4,552,000	101	78 = 98	24 = 105	4,210,000	93	78 = 98	26 = 102	5,120,000
Margherita Hut, 4560 m, Aug. 3, immediately after arrival	102	70 = 88	27 = 103	—	108	84 = 105	22 = 108	—	102	80 = 100	26 = 103	—	94	70 = 85	26 = 103	—
Margherita Hut, 4560 m, Aug. 4	92	67 = 85	37 = 89	—	96	80 = 100	27 = 103	—	106	80 = 100	29 = 100	—	96	76 = 95	29 = 98	—
Margherita Hut, 4560 m, Aug. 5, after mountain climbing	90	62 = 78	—	—	—	—	—	—	96	67 = 84	—	—	—	—	—	—
Margherita Hut, 4560 m, Aug. 5, afternoon	88	65 = 81	—	—	104	85 = 106	26 = 103	—	98	76 = 96	29 = 99	—	102	72 = 90	27 = 101	—
Colle d'Olen, 2900 m, Aug. 8	—	—	—	—	104 103	—	25 = 104	5,176,000	—	[illegible]5 = 105	27 = 103	—	97	82 = 102	27 = 101	5,536,000
Colle d'Olen, 2900 m, Aug. 11	97	77 = 96	36 = 85	4,848,000	105	80 = 100	28,5 = 100	5,408,000	102	80 = 100	28,5 = 100	4,821,000	—	—	—	—
Heidelberg, Sept. 13	—	—	—	—	—	84 = 105	19 = 100	5,064,000	—	80 = 100	26 = 102 27 = 103	5,000,000	—	80 = 100	27 = 101	5,544,000

/70.71

however, domesticated animals move about so little that the heat regulation by water evaporation plays no major role here.

We made blood tests on two dogs that had been shipped from Turin to Varallo (451 m). In the larger fully grown dog, we tested only blood taken from the ear vessels.

TABLE II /71

	Haldane	Sahli	A. and K.	Erythrocytes
Varallo	95	—	—	—
Colle d'Olen 1st day	93	70:88	26:103	—
" " 11th day	96	77:96	31:96	6,352,000

In the smaller young dog, we took blood from the ear in Varallo and during the first experiment on the Colle d'Olen, while blood from the carotid artery was used in the second experiment on the Colle d'Olen.

TABLE III

	Haldane	Sahli	A. and K.	Erythrocytes
Varallo	—	42:53	—	—
Collo d'Olon 1st day	48	45:56	69:45	—
" " 8th day	50	38:48	70:47	3,056,000
	—	38·48	—	—

This means that, also in the dog, no increase in hemoglobin and erythro- /72 cytes, or only a very negligible increase, is observed. In the smaller dog, the carotid blood was used for the following additional experiment: The blood was defibrinated and the hemoglobin was determined with the various apparatus available. For comparison, we diluted 10 cc blood with physiological salt solution, centrifuged the erythrocytes off, and washed the preparation with salt solution on the centrifuge. Then, the erythrocytes were diluted with water and, under addition of a large amount of sodium chloride, were coagulated by boiling with a small amount of acetic acid. The coagulate was washed free of chlorine with water, shaken with alcohol and ether, dried in the drier to weight constancy, and then weighed. The coagulate weighed 0.721 gm. As mentioned above, the Haldane and Sahli figures can be used for calculating the hemoglobin content. According to Haldane (50), 0.69 gm hemoglobin should be present in 10 cc blood, while the corresponding value according to Sahli (38) should be 0.67 gm. In addition to the hemoglobin, the erythrocytes contain small amounts of stroma protein so that the slightly too high hemoglobin content is not surprising; the agreement is fairly satisfactory and the apparatus readings themselves coincide very well.

To obtain definite data on the increased water dissipation in human subjects at higher altitudes, we made a number of weighings, in the evening and morning. At higher altitudes, the weight loss was greater than at sea level. The figures are combined with those of 1909 in Table IV.

The main result of our blood tests is the fact that, also in this case in which we worked with different methods, no hemoglobin rise on stay in the high mountains was observed. This confirms the results obtained by Cohnheim, Kreglinger, Masing, and Morawitz, so that it can be definitely stated that at altitudes of 2900 and 4500 m, over an experimental period of two weeks, no physiological hemoglobin increase takes place in either human subjects or dogs. Im- /73 mediately after strenuous mountain climbing, we observed a decrease in hemoglobin content, as had already been reported by Cohnheim and Kreglinger. Until now, this phenomenon has been observed only in mountainous terrain. This agrees with the statements by Bürker, to the effect that the blood is extremely labile in high mountains.

TABLE IV

	Cohnheim	Kreglinger	Tobler	Weber
Lowland	360	320		—
	211	150	In numerous determinations fluctuating between	—
	300	300		—
	243	—		—
	292	—		—
	350	—		—
	243	—	150—300	—
	295	—		—
Colle d'Olen	330	650	150	300
	510	350	750	400
	100	550	—	—
	330	—	—	—
	400	—	—	—
Margherita Hut	350	200	450	325
	225	600	300	350
	150	500	250	300
	390	400	—	—
	340	250	—	—
	350	300	—	—

The negative result of these blood tests agrees with the determinations of the oxygen consumption, made by Durig and coworkers (Bibl.30, specifically pp.293 and 349). The oxygen consumption was distinctly increased at high altitudes but did not vary even on extended stay (several weeks); similarly, the partial pressure of oxygen and carbon dioxide in the alveolar air remained constant during the entire time. Douglas and Ward also were unable to observe an adaptation /74 of the respiratory metabolism to altitude conditions. Apparently, the human organism has no regulatory mechanisms for compensating the decreased oxygen pressure. Incidentally, it is by no means certain that a hemoconcentration actually constitutes a useful regulation; in any case, it has never been encountered. Naturally, despite these negative findings, it is not impossible that a change in blood composition might occur after years of staying at higher altitudes. The older French findings by Bert and Viault have never been substantiated.

Just as some other authors, we observed a distinct altitude effect in self-experiments. The effect was not too extensive at the Colle d'Olen although we all came directly from the lowland and were untrained. The only noticeable symptom was an increase in fatiguability of the respiratory muscles, observed while cleaning and blowing the pipettes. However, on the ascent to the Margherita Hut and during the stay there, symptoms of dyspnea, frequently described since Saussure's time, were observed. Already after relatively mild exertion, we were fatigued and short of breath; both symptoms disappeared again after brief resting periods. During the last ascent from the firn field to the hut, we had to stop every 60 - 100 steps. In the hut, even bending down caused dyspnea. During the rest period, especially at night, all participants experienced changes in well-being, with occasional headaches, insomnia, and attacks of palpitation. At times, reluctance to perform physical exertion became pronounced. Surprisingly, Cohnheim who had suffered the least in our experiments two years previously, showed the greatest effect whereas Kreglinger was less affected than two years before. These disorders probably cannot be considered pure altitude effects; possibly, the antiphysiological state of the physiological laboratory on the Margherita Hut, specifically the small and poorly ventilated dormitory, may have been in part responsible.

Cohnheim and Kreglinger (Bibl.18) observed as early as 1909 that profuse /75 perspiration will lead to such a chlorine loss that a strong chlorine retention must necessarily occur on the following days, to replenish the depleted reserves; in addition, the chlorine reserves of the body may be so much exhausted by strong perspiration that the hydrochloric acid secretion of the stomach will be impaired. In our newest experiments, we scheduled an investigation of the consequences of intense sodium chloride loss through perspiration, with respect to the water metabolism of the body. Our program consisted in producing profuse perspiration by several mountain climbings and in replacing this chlorine by adjustment of the diet in a part of the experiment and living on a chlorine-free diet for the remainder of the experiments. We scheduled to study the excretion of water and sodium chloride as well as the behavior of the body weight.

TABLE V

	NaCl gm
1 slice bread (63 - 69 gm)...........	0.6
1 tbs. condensed milk	0.19
1 canned sardine	0.29
5 cc Brodo (concentrated meat broth).	0.3
100 gm ham	4.7
100 gm ham fat	0.67

In part, the sodium chloride was added to the food; occasionally, we had to eat chlorine-containing foodstuffs whose chlorine content had to be determined first. For this, portions of the food were ashed in the moist state, using the Neumann method; the liberated hydrochloric acid was absorbed in silver nitrate, and the chlorine was titrated according to the Volhard process. The data are given in sodium chloride. The contents are given in Table V.

The chlorine content of the other foodstuffs (fresh meat, sugar, chocolate, macaroni, canned fruit) was disregarded. The drinking water (melted snow) /76 was completely free of chlorine. The chlorine content in the urine was titrated according to Volhard (Weber) and is given as sodium chloride.

We made the following experiments: On July 31, we climbed from Alagna to the Colle d'Olen on the afternoon and evening, usually in the shade. The altitude difference was 1700 m; the time required was 4 h 55 m and all four of us ate 20 gm sugar and crackers and drank 280 cc tea (Weber, 330 cc). Table VI gives the observed weight loss and the weight loss calculated on the basis of the ingested food, i.e., the true loss from the body. In addition, the percent of sodium chloride and the absolute content of sodium chloride are given for the urine of the following night.

TABLE VI

	Weight Loss gm	Calculated Loss gm	Urine cc	NaCl %	NaCl gm
Cohnheim	1800	2100	350	1.25	4.3
Kreglinger	1800	2100	320	1.2	3.84
Tobler	1200	1500	295	1.6	4.8
Weber	1500	1850	175	1.1	1.93

On Aug.3, we ascended from the Laboratory to the Margherita Hut. The weather was sunny with a light breeze; for this reason, the perspiration losses were somewhat lower than during the ascent in 1909. We started at 4:30 AM, arriving at the Gnifetti Hut at 7:25 - 7:58 and at the Lysjoch at 10:08 - 10:35. Arrival at the top was at 12:21 PM, i.e., a total hiking time of 6 h 51 m, with a time difference between the individual weighings of about 9 hrs. On the afternoon of Aug.3, we installed the testing laboratory; on Aug.4, we rested mostly and did some laboratory work. On both days, our diet contained a weighed more or less normal amount of chlorine. After Aug.5, we lived on a low-salt diet. On Aug.5, Kreglinger and Tobler ascended the Dufour peak. They took /77
6.5 hrs, of which 5.5 were spent in actual climbing. Throughout the period, there was sunshine but a cold wind, so that the perspiration losses were minimal. Since the wind did not stop, the two others did not climb the Dufour peak on the

next day while the descent of the first two took place on Aug.6, during which time they only drank tea. The low-chlorine diet was continued until Aug.7. The results were as follows:

Cohnheim. Ascent: weight loss 3200 gm; 670 gm liquid, 400 gm solid food, 530 cc urine, 120 gm feces; calculated loss, 3620 gm.

Aug.3, afternoon: 10.4 gm sodium chloride intake;

Aug.4: 14 gm sodium chloride intake;

Aug.3, afternoon: 218 cc urine, 1% NaCl, 2.2 gm NaCl;

Aug.3 evening to Aug.4 afternoon: 933 cc urine, 0.86% NaCl, 8.0 gm NaCl;

Aug.4 afternoon to Aug.5 morning: 830 cc urine, 0.86% NaCl, 7.1 gm NaCl;

Low-chlorine diet:

Aug.5 morning to Aug.6 morning: 1.1 gm intake, 980 cc urine, 0.93% NaCl, 9.1 gm NaCl;

Aug.6 morning to Aug.7 morning: 1.5 gm intake, 530 cc urine, 0.53% NaCl, 2.8 gm NaCl;

Descent: weight loss 950 gm; calculated loss, 1100 gm.

Kreglinger. Ascent: weight loss 1650 gm; 515 gm liquid, 385 gm solid food, 290 cc urine; calculated weight loss, 2250 gm.

Aug.3, afternoon: 10.4 gm NaCl intake;

Aug.4: 14.0 gm NaCl intake;

Aug.3, afternoon: 320 cc urine, 0.94% NaCl, 3.0 gm NaCl;

Aug.3 evening to Aug.4 afternoon: 608 cc urine, 1.1% NaCl, 6.9 gm NaCl;

Aug.4 evening to Aug.5 morning: 306 cc urine, 1.4% NaCl, 4.35 gm NaCl.

Low-chlorine diet:

Aug.5 morning to Aug.6 morning: 1.2 gm intake, 760 cc urine, 1.22% NaCl, 9.27 gm NaCl;

Aug.6 morning to Aug.7 morning: 2.1 gm intake, 750 cc urine, 0.57% NaCl, 4.3 gm NaCl;

Aug.5, mountain climbing: weight loss 550 gm; 300 gm solid food, 880 gm liquid, 260 cc urine; calculated weight loss, 1470 gm;

Aug.6, descent: weight loss, 550 gm; calculated loss, 700 gm. /78

Tobler. Ascent: weight loss, 1650 gm, 360 cc urine, 535 gm liquid, 365 gm solid food; calculated loss, 2190 gm.

Aug.3, afternoon: 10.8 gm NaCl intake;

Aug.4: 12.1 gm NaCl intake;

Aug.3, afternoon: 275 cc urine, 1.4% NaCl, 3.88 gm NaCl;

Aug.3 evening to Aug.4 afternoon: 602 cc urine, 1.2% NaCl, 7.3 gm NaCl;

Aug.4 evening to Aug.5 morning: 490 cc urine, 1.06% NaCl, 5.2 gm NaCl.

Low-chlorine diet:

Aug.5 morning to Aug.6 morning: 1.2 gm intake, 675 cc urine, 1.13% NaCl, 7.6 gm NaCl;

Aug.6 morning to Aug.7 morning: 2.1 gm intake, 660 cc urine, 0.6% NaCl, 4.0 gm NaCl;

Aug.5, mountain climbing: weight loss, 950 gm, 280 cc urine, 80 gm feces, 250 gm solid food, 510 gm liquid; calculated loss, 1350 gm.

Aug.6, descent: weight loss, 550 gm; calculated loss 625 gm.

Weber. Weight loss, 2000 gm; 750 gm liquid, 280 gm solid food, 450 cc urine; calculated loss, 2580 gm.

Aug.3, afternoon: intake, 6.9 gm NaCl;

Aug.4: intake, 4.8 gm NaCl;

Aug.3, excretion: no urine in the afternoon;

Aug.3 evening to Aug.4 afternoon: 950 cc urine, 0.67% NaCl, 6.37 gm NaCl;

Aug.4 afternoon to Aug.5 morning: 550 cc urine, 1.07% NaCl, 5.9 gm NaCl.

Low-chlorine diet:

Aug.5 morning to Aug.6 morning: 1.4 gm intake, 970 cc urine, 0.56% - 5 4 gm NaCl;

Aug.6 morning to Aug.7 morning: 2.1 gm intake, 490 cc urine, 0.28% NaCl, 1.4 gm NaCl.

Descent: weight loss, 600 gm; calculated loss, 750 gm.

On Aug.10, we undertook a climbing expedition around the Corno Rosso and to the Punta Straling; the descent took place to Lake Gabiet, where we swam in the lake and then returned to the Laboratory. In all, we were 10 hrs on the /79 way and lived on a low-salt diet on this and on the following days.

Cohnheim. Weight loss, 3350 gm; 282 cc urine, 2315 gm liquid, 420 gm solid food; calculated loss, 5800 gm. Urine until evening, 69 cc, 0.43% NaCl, 0.3 gm NaCl;

Nighttime: 390 cc urine, 0.11% NaCl, 0.4 gm NaCl;

Aug.11 - 12, morning: 700 cc urine, 0.05% NaCl, 0.35 gm NaCl;

Aug.10: 0.9 gm intake;

Aug.11: 0.9 gm NaCl intake;

Kreglinger. Weight loss, 3000 gm; 40 cc urine, 680 gm liquid, 250 gm solid food; calculated loss, 3900 gm. Urine until Aug.11 in the morning, 640 cc, 0.45% NaCl, 2.9 gm NaCl;

Aug.11 - 12, morning: 820 cc urine, 0.22% NaCl, 1.8 gm NaCl;

Aug.10: 1.0 gm intake;

Aug.11: 0.9 gm NaCl intake.

Tobler. Weight loss, 2800 gm; 175 cc urine, 840 gm liquid, 370 gm solid food; calculated loss, 3730 gm;

Urine to evening, 205 cc, 1.05% NaCl, 2.15 gm NaCl;

Urine at night, 210 cc, 0.22% NaCl, 0.46 gm NaCl;

Aug.11 - 12, morning: 705 cc urine, 0.28% NaCl, 1.97 gm NaCl;

Aug.10: 0.9 gm NaCl intake;

Aug.11: 0.9 gm intake.

The fourth of us (Weber) was forced to leave suddenly on the evening of Aug.9, for professional reasons, and could not participate in this climb.

The figures for the intake and excretion of sodium chloride, immediately after ascent to the Margherita Hut, i.e., during a high-salt diet, showed a strong chlorine retention (exactly as in the experiments of 1909), obviously having the function of replenishing the chlorine lost through the perspiration. Our data and those of 1909 are compiled in Table VII. The figures refer to the afternoon of the ascent and to the following day, up to the morning thereafter. On that morning, we changed to a low-salt diet since, according to the experience gained in 1909, a substantial chlorine retention was no longer to be expected after the third day. The calculated loss is entered for each test /80 subject.

This retention would be even more pronounced, except for the peculiar

TABLE VII

	Intake	Excretion	Retention	Calculated Loss
Cohnheim 1909	18.5	10.35	8.15	4000
" 1911	24.4	17.3	7.1	3620
Kreglinger 1909	21.5	10.9	10.6	3870
" 1911	24.4	14.25	10.15	2250
" II. 1909	18.5	4.17	14.33	5800
Kestner 1909	18.5	8.68	9.82	4100
Tobler 1911	22.9	16.4	6.5	2190
Weber 1911	17.7	12.3	5.4	2580

phenomenon that the kidneys, even in the face of a chlorine deficiency, continue to secrete chlorine. The above data clearly prove this point. After the first ascent to the Colle d'Olen, on a regular diet, the urine contained 1.1 - 1.6% NaCl; the urine of Aug.3 and 4, i.e., during chlorine retention, still contained 1% sodium chloride. Even in the case of an almost salt-free diet, the sodium chloride values remained above 0.5% and decreased only slowly. On Aug.10 and 11, salt deficiency and salt losses combined so that the total content dropped to 0.3, 0.22, and 0.05% but then remained at this level, meaning that the kidney activity further impaired the physical state of the body and removed still more chlorine from the already depleted reserves. Grünwald (Bibl.31) had proved on rabbits that the sodium chloride excretion does not stop on depletion of salt reserves. Diuresis will increase the chlorine excretion and thus may become harmful to the animal body. It seems that the secretion of an entirely salt-free urine is a function difficult to perform by the kidney, a fact which should be taken into consideration in any theory on renal function.

As mentioned above, we planned to study the behavior of water during chlorine deficiency. Clinical data collected over recent years have indicated /81 that sodium chloride and water are intimately connected in the body functions.

One of us (Tobler) made animal experiments (Bibl.32) and experiments on infants (Bibl.33) in which he studied the behavior of the body water and salts during sudden weight losses which, as is generally known, are mainly due to water loss. Tobler differentiated three phases of water dissipation: A portion of the water may be excreted by the body without entraining other substances, which will lead to a concentration of the tissue fluids. Tobler designated this portion as "water of concentration". A second portion of the water is excreted by the body, together with a certain amount of salt; experience in pediatrics has shown that this water can be reabsorbed by the body only in combination with the corresponding amount of salts, specifically of sodium chloride. This portion was designated by Tobler as "water of reduction". A third portion of water can be excreted by the body only under concomitant destruction of the body tissues, and no compensation of the loss within a short period of time is possible. Tobler designated this portion as "water of destruction". This latter portion naturally is not in question in healthy individuals with unlimited water intake; conversely, the second portion is very much in question. During perspiration, the water excreted by the body is not pure water but a combination of water and sodium chloride. This raised the question as to the behavior of the organism if no sodium chloride were offered for compensating these weight losses; to settle the question, we investigated our body weights at ordinary, i.e., high-salt, and at low-salt diet, in which weight losses were induced by perspiration which the body then tried to make up again during the subsequent days. The weight losses by perspiration, including directly observed losses and calculated losses, were given above. The rate of weight recovery is shown in Table VIII. The upper figures, until Aug.5 (up to the horizontal line) /82 refer to a chlorine-containing diet, while the figures below this line refer to a chlorine-free diet. The weighings were made without clothing.

An elimination of sodium chloride from the diet, as is generally known, will lead to a weight loss even without perspiration; on Aug.5 and 6 we actually observed a slight weight loss in Cohnheim and Weber who had done no work on Aug.5. The loss was much more distinct in the two other subjects who had climbed the Dufour peak on this day. Another loss was observed in all four subjects on Aug.6, during the ascent to the Colle d'Olen. Cohnheim did not feel well on this day and thus ate less. A considerable weight loss was produced by the climb to the Punte Straling. As mentioned above, Weber did not participate in this; the three others had accompanied him on the preceding evening to the Alp Sevii and then returned to the laboratory. The difference in altitude is about 1000 m, and this hike was the reason for the fact that the morning weight on Aug.10 had not yet returned to its previous level. Therefore, the weight losses, on the following day, on a chlorine-free diet, start below the zero point; the curves are less distinct but the chlorine depletion was better substantiated. In the accompanying diagram, the course of the weights is plotted; the solid lines refer to a chlorine-containing and the broken lines to a chlorine-free diet.

The curves, even more distinctly than the Table, show the great difference in the slope of the weight curve for chlorine-containing and chlorine-free diets. In the chlorine-containing diet, the drop in weight, no matter how large, is recovered completely or almost completely by the next morning. Frequently, the initial weight is exceeded during a day of rest, presumably because of the increase in muscle tissue after muscular exertion. In low-salt diets, the weight losses due to perspiration cannot be compensated. The weight re-increases only slowly, despite water intake and despite unlimited food intake. Consequently,

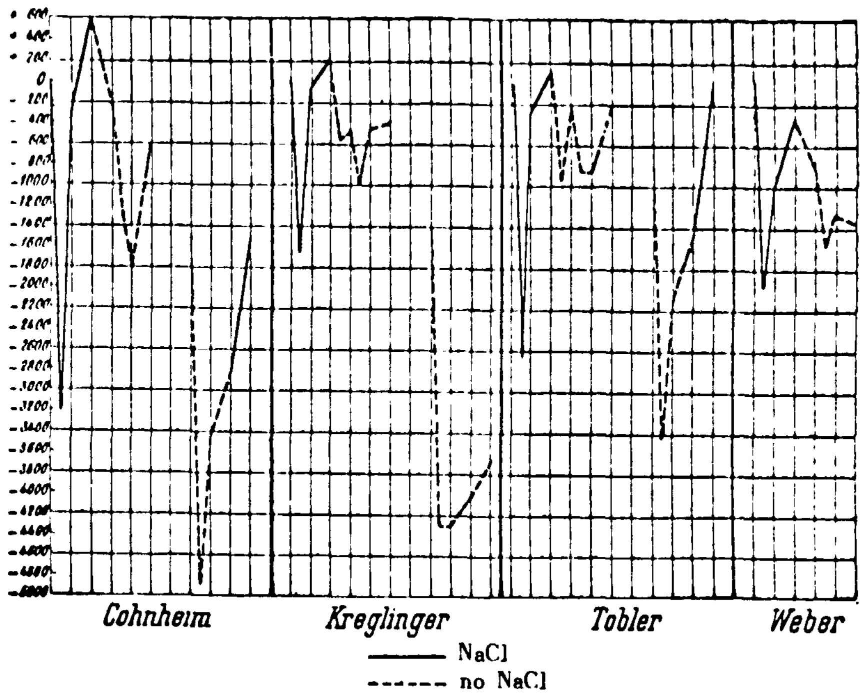
TABLE VIII

	Cohnheim		Kreglinger		Tobler		Weber		
Aug. 2, morning...	85 000	—	78 500	—	65 300	—	64 200	—	
Aug. 3, morning...	84 400	(in. w.)*	78 800	(in. w.)*	64 900	(in. w.)*	64 500	(in. w.)*	
1 PM	81 200	(— 3200)	77 150	(— 1650)	62 250	(— 2650)	62 500	(— 2000)	Work
evening...	84 350	—	79 050	—	65 300	—	64 150	—	
Aug. 4, morning...	84 100	(— 300)	78 650	(— 150)	64 600	(— 300)	63 500	(— 1000)	Rest
evening...	85 550	—	79 250	—	65 300	—	64 500	—	
Aug. 5, morning...	85 200	(+ 800)	79 000	(+ 200)	65 000	(+ 100)	64 150	(— 350)	"
Aug. 5, 1 PM	—	—	78 450	(— 550)	64 050	(— 950)	—	—	Work Rest
evening...	84 500	—	78 800	—	64 900	—	63 950	—	
Aug. 6, morning...	84 150	(— 250)	78 500	(— 500)	64 650	(— 250)	63 650	(— 850)	
noon	83 100	(— 1300)	77 800	(— 1000)	64 000	(— 900)	62 900	(— 1600)	Work
Aug. 7, morning...	82 600	(— 1800)	78 350	(— 450)	64 000	(— 900)	63 200	(— 1300)	
evening...	84 500	—	79 650	—	66 300	—	64 200	—	Rest
Aug. 8, morning...	83 800	(— 600)	78 400	(— 400)	64 700	(— 200)	63 150	(— 1350)	
			(900 cc night urine)		(850 cc night urine)		(650 cc night urine		
Aug. 10, morning..	82 900	(— 1500)	77 400	(— 1400)	64 050	(— 850)	—	—	Work
evening..	79 550	(— 4850)	74 450	(— 4350)	61 450	(— 3450)	—	—	Rest
Aug. 11, morning..	80 975	(— 3125)	74 450	(— 4350)	62 800	(— 2100)	—	—	
Aug. 12, morning..	81 600	(— 2800)	74 750	(— 4050)	63 400	(— 1500)	—	—	
Aug. 13, morning..	82 900 [1]	(— 1500)	75 100	(— 3700) [2]	64 900 [1]	(— 0)	—	—	

[1] Salt intake. [2] No salt intake.

* in.w. = initial weight.

losses due to perspiration have the same result as those obtained in the weight drops found by Tobler, meaning that the water of reduction can be replaced only if the corresponding amount of salt is simultaneously supplied. /84



These investigations explain two phenomena which had never been fully understood. Zuntz and Schumburg (Bibl.34), during strenuous exercise connected with profuse perspiration, observed excretion of large quantities of highly dilute urine. They assumed that this removes toxic material from the body, which had been formed during muscular work. On the basis of our observations, we assume that this constitutes the excretion of water which had been drunk /85 to still existing thirst but could not be converted by the body because of a deficiency of salt intake. On Aug.8 in the morning, i.e., after the first night following the chlorine-low period, we observed the excretion of extremely large amounts of urine, obviously due to the increased water intake during extreme thirst, which could not be retained in the body because of the lack of the necessary salt. This is directly connected with a second phenomenon, observed by many mountain climbers and tourists, specifically during the initial period of their climb. It will not happen to the more experienced tourist, but novices occasionally exert themselves excessively and quench their thirst by drinking water wherever they see a spring or brook without, however, truly satisfying their thirst. Rather, as the popular saying goes, the more one drinks the more thirsty one becomes. Obviously, this is due to the fact that, because of the excessive salt loss with the perspiration, the lost water of reduction cannot be assimilated again. As soon as food is taken, which usually supplies some salt, the thirst will be quenched. While hiking, however, it is difficult to still one's thirst, because of the lack of salt. We made an attempt to eat an increased amount of salt during strenuous mountain climbing and had the subjective feeling that our thirst was easier to quench.

If our interpretation of this latter phenomenon is correct, an interesting conclusion for the general sensation of thirst could be drawn, namely, that this sensation has to do with the conditions of the water reserves in the body rather than with an increased concentration of the blood.

A study of the curves shows that, despite the chlorine deficiency, the assimilation of the water in the body is not completely canceled. The broken lines, corresponding to a chlorine-low diet, rise more slowly than the normal /86
curves, but do show an increase. This means that, to a certain extent, the body is able to assimilate water without the corresponding amount of salt, the so-called water of concentration mentioned by Tobler. In defining the water of concentration, it follows that water and salt are not at an absolutely rigid ratio. If one would subscribe to the older concepts as to the presence of salt solutions as liquids, a change in the osmotic pressure of this liquid would have to be possible. The much more logical concept by M.H.Fischer (Bibl.35)

who considered the water as being bound to the colloids as swelling water, believed that the salt influences the amount of bound water. Our experiments indicate that an independence exists within certain limits.

Another consequence of salt loss had been observed originally by Cohnheim and Kreglinger. They found that the gastric hydrochloric acid secretion is reduced because of the chlorine losses. Tobler and Cohnheim (Bibl.36, 37), in experiments on dogs, found that chlorine losses readily interfere with the hydrochloric acid secretion; Rosemann and Herrmannsdorfer (Bibl.38, 39) were able to confirm these findings on a voluminous experimental material. In human subjects, the salt reserves are relatively large (Bibl.40) but practical experience gained at that time indicated that these reserves can be exhausted by profuse perspiration. Another consequence of reduced gastric hydrochloric acid secretion should be mentioned here (Bibl.41). If the secretion of the acid gastric juice becomes less, the body loses the ability of de-acidification and thus shifts the equilibrium of the juice toward the alkaline side. The de- /87 acidification of the body by the gastric juice secretion has the function of counteracting body fatigue which is partly accompanied by the formation of lactic acid in the muscles; no doubt, some of the fatigue symptoms after strenuous muscular work have to do with these findings.

The assumption of such a correlation is specifically substantiated by conditions in high mountains where, according to the findings by Galeotti and Barcroft (Bibl.42, 43), organic acids - predominantly lactic acid - are formed in the blood. We are able to contribute to the knowledge on the occurrence of such substances in the urine. Cohnheim and Kreglinger observed that their urine, after strenuous exercise at high altitudes, reduced permanganate; we repeated this test. A total of 10 cc urine was mixed with 3 gm conc. sulfuric acid, to which gradually 1% solution of potassium permanganate was added until the permanganate was just about reduced. Table IX shows the results, in which the figures give the cubic centimeters of permanganate solution.

TABLE IX

	Cohn-heim	Kreg-linger	Tobler	Weber
Aug. 3, ascent	17	17	17	—
Aug. 3-4, night	16	27	26	15
Aug. 4-5, rest	—	24	—	—
Aug. 5-6, rest	14	—	—	9
Aug. 5-6, ascent	—	24	24	—
Aug. 6-7, rest	24	22	19	16
Aug. 10-11, ascent	39	37	42	—
Aug. 10-11, night urine	39	—	37	—
Aug. 11-12, rest	18	9	28	—
Aug. 12-13, rest	12	11	21	—

We suspected first that substances of the acetone group were involved /88 here and therefore mixed that portion of urine which showed especially strong reductions with iodine solution and sodium hydroxide. There was a slight odor of iodoform; on longer standing, a slight yellowish precipitate formed. However, the quantity in question can only be extremely slight. In 50 cc urine, we titrated the consumption of iodine with thiosulfate, according to Embden's instruction (Bibl.44); however, the consumption barely exceeded the error limits. The urines showed negative sugar reaction, and the observations by Barcroft seem to indicate that lactic acid was in question here.

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